Journal of Cardiology 66 (2015) 57–62

Contents lists available at ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Original article

Long-term outcomes of septal reduction for obstructive hypertrophic cardiomyopathy

Daniel Sedehi (MD), Gherardo Finocchiaro (MD)*, Yen Tibayan (MD), Jeffrey Chi (MD), Aleksandra Pavlovic (BS), Young M. Kim (DPhil), Frederick A. Tibayan (MD), Bruce A. Reitz (MD), Robert C. Robbins (MD), Joseph Woo (MD), Richard Ha (MD), David P. Lee (MD), Euan A. Ashley (MRCP, DPhil)*

Division of Cardiovascular Medicine, Stanford University Medical Center, Stanford, CA, USA

ARTICLE INFO

Article history:
Received 25 November 2013
Received in revised form 16 July 2014
Accepted 14 August 2014
Available online 18 September 2014

Keywords:
Hypertrophic cardiomyopathy
Septal myectomy
Alcohol septal ablation
Long-term outcomes

ABSTRACT

Background: Surgical myectomy and alcohol septal ablation (ASA) aim to decrease left ventricular outflow tract (LVOT) gradient in hypertrophic cardiomyopathy (HCM). Outcome of myectomy beyond 10 years has rarely been described. We describe 20 years of follow-up of surgical myectomy and 5 years of follow-up for ASA performed for obstructive HCM.

Methods: We studied 171 patients who underwent myectomy for symptomatic LVOT obstruction between 1972 and 2006. In addition, we studied 52 patients who underwent ASA for the same indication and who declined surgery. Follow-up of New York Heart Association (NYHA) functional class, echocardiographic data, and vital status were obtained from patient records. Mortality rates were compared with expected mortality rates of age- and sex-matched populations.

Results: Surgical myectomy improved NYHA class (2.74 ± 0.65 to 1.54 ± 0.74, $p < 0.001$), reduced resting gradient (67.4 ± 43.4 mmHg to 11.2 ± 16.4 mmHg, $p < 0.001$), and inducible LVOT gradient (98.1 ± 34.7 mmHg to 33.6 ± 34.9 mmHg, $p < 0.001$). Similarly, ASA improved functional class (2.99 ± 0.35 to 1.5 ± 0.74, $p < 0.001$), resting gradient (67.1 ± 26.9 mmHg to 23.9 ± 29.4 mmHg, $p < 0.001$) and provoked gradient (104.4 ± 34.9 mmHg to 35.5 ± 38.6 mmHg, $p < 0.001$). Survival after myectomy at 5, 10, 15, and 20 years of follow-up was 92.9%, 81.1%, 68.9%, and 47.5%, respectively. Of note, long-term survival after myectomy was lower than for the general population [standardized mortality ratio (SMR) = 1.40, $p < 0.005$], but still compared favorably with historical data from non-operated HCM patients. Survival after ASA at 2 and 5 years was 97.8% and 94.7%, respectively. Short-term (5 year) survival after ASA (SMR = 0.61, $p = 0.48$) was comparable to that of the general population.

Conclusion: Long-term follow-up of septal reduction strategies in obstructive HCM reveals that surgical myectomy and ASA are effective for symptom relief and LVOT gradient reduction and are associated with favorable survival. While overall prognosis for the community HCM population is similar to the general population, the need for surgical myectomy may identify a sub-group with poorer long-term prognosis. We await long-term outcomes of more extensive myectomy approaches adopted in the past 10 years at major institutions.

Introduction

Hypertrophic cardiomyopathy (HCM) is the most common monogenic cardiovascular disease. The obstructive form of HCM is particularly associated with symptoms and exertional limitation. Further, the presence of left ventricular outflow tract (LVOT) obstruction predicts increased mortality in HCM [1,2]. Accordingly, interventional therapies that aim to decrease LVOT gradient, either surgically or percutaneously have recently arisen. The long-term impact of such septal reduction therapies has been little studied.

Surgical myectomy was first described by Andrew Glenn Morrow in 1961 and is the gold-standard treatment for medically refractory obstructive HCM [3]. Surgeons at Stanford Hospital have performed myectomy since 1972. In 1996, Robbins and colleagues

* Corresponding authors at: Center for inherited cardiovascular disease, Stanford School of Medicine, 300 Pasteur Drive, CVRB 277, Stanford, CA 94305, USA. Tel.: +1 650 498 4900; fax: +1 650 725 1599.
E-mail addresses: gherardobis@yahoo.it (G. Finocchiaro), euan@stanford.edu (E.A. Ashley).

http://dx.doi.org/10.1016/j.jjcc.2014.08.010
0914-5087/

[4] described mid-term outcomes, and demonstrated myectomy to be a safe and effective modality that improves New York Heart Association (NYHA) functional class and symptoms. Others have also reported mid-term follow-up for myectomy outcomes [5,6]. In the mid-1990s, alcohol septal ablation (ASA) emerged as an alternative interventional strategy for some patients with symptomatic obstructive HCM [7,8]. In non-randomized studies, both myectomy and ASA markedly improved functional classification and effectively reduced LVOT gradient [9–13].

In this paper, we report 20 years of post-procedural survival for patients who underwent surgical septal reduction therapy between 1972 and 2006 along with 5-year post-procedural survival for those who underwent catheter-based alcohol septal reduction. We compare long-term outcome with the expected survival in the general population.

Methods

At Stanford University Medical Center between January 1972 and December 2006, 282 patients with severe medically refractory symptoms resulting from obstructive HCM underwent intervention for LVOT. For the surgical cohort, we chose to study the 192 patients who underwent an isolated surgical myectomy without concomitant surgical procedure (most commonly mitral valve repair or replacement). Twenty-one patients were lost to follow-up after myectomy, leaving 171 patients in the isolated myectomy cohort. ASA was first performed at our institution in 2002. From January 2002 to December 2006, 52 patients underwent ASA because of co-morbidity or patient preference. No ASA patients were lost to follow-up.

The diagnosis of HCM was based on standard clinical and echocardiographic features, including myocardial hypertrophy in the absence of other possible etiology. Before 1978, direct pressure measurements were used to determine the degree of outflow tract gradient. Since 1978, the degree of myocardial hypertrophy was routinely assessed with M-mode echocardiography. Since 1984, two-dimensional transthoracic echocardiography and continuous-wave Doppler have been used. In accordance with American Society of Echocardiography (ASE) guidelines, M-Mode, and 2D methods of echocardiography were used in assessing left ventricular (LV) diameters, shortening fraction, intraventricular septum, and LV posterior wall thickness, and left-atrial end-systolic diameter. Left ventricular hypertrophy was assessed and measured in end-diastole using 2D echo (Fig. 1) [14].

HCM without significant symptoms or without significant (>30 mmHg) resting or provokable LVOT gradient (during Valsalva or exercise) was considered a contraindication for septal reduction therapy. Prior to intervention and after extensive discussion of treatment options, including risks and limitations, written informed consent was obtained for all procedures.

The investigation conforms with the principles outlined in the Declaration of Helsinki [15], and with the local legal requirements and was approved by the Institutional Review Board at Stanford.

Although more recently a transition has been made toward more extensive myectomy, for most patients in this historical cohort septal myectomy was performed as described by Robbins

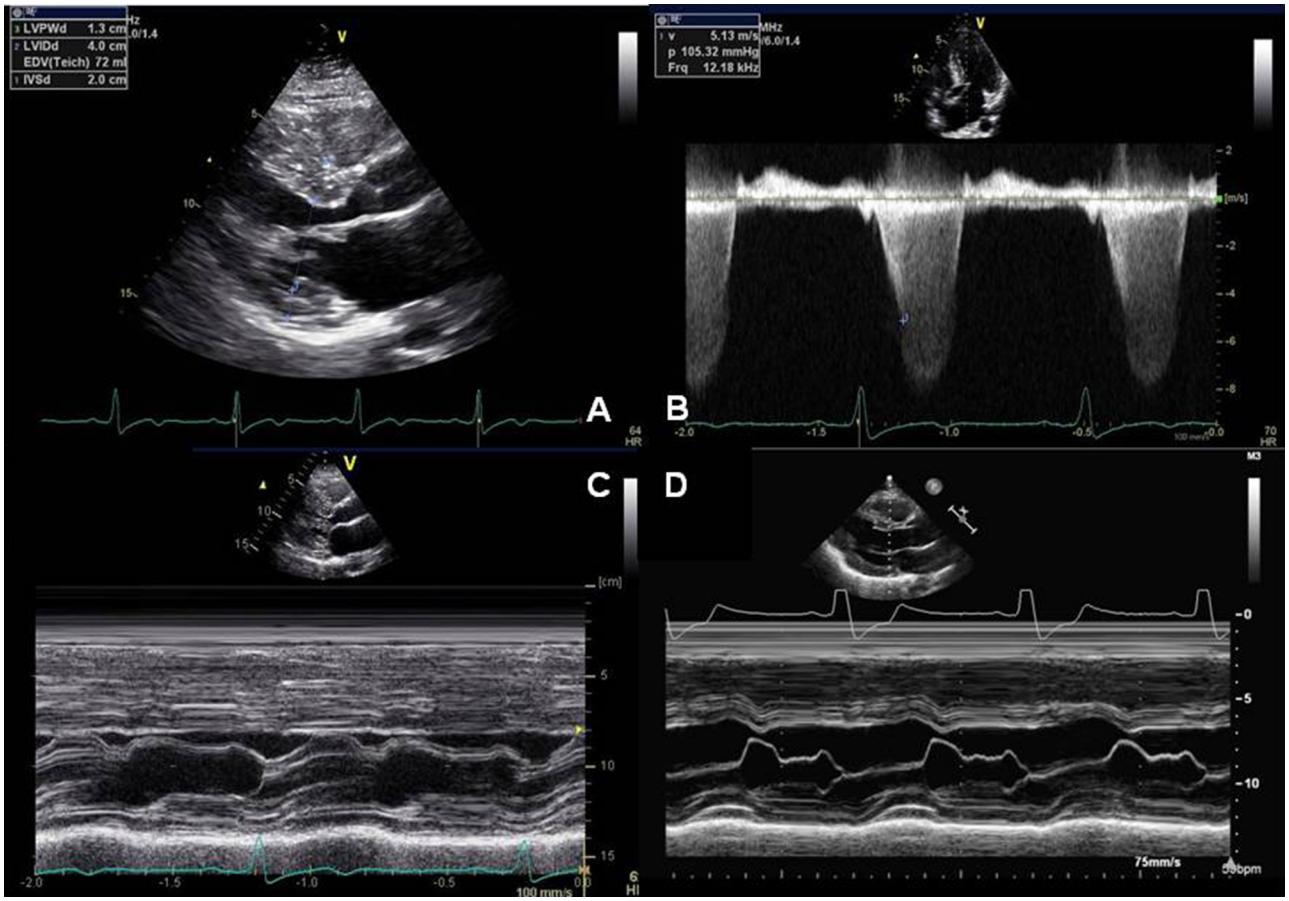

Fig. 1. Echocardiographic assessment in hypertrophic cardiomyopathy (HCM). Parasternal long-axis showing asymmetric hypertrophy (A); continuous wave Doppler in a patient with obstructive HCM (B); M-mode of the left ventricle at the mitral valve level in a patient before (C) and after (D) a septal myectomy, demonstrating presence and absence of systolic anterior motion.

and colleagues [4]. In brief, an oblique aortotomy is made, and the right coronary cusp of the aortic valve is retracted to expose the interventricular septum. Two parallel incisions are made in the septum, beginning 3–5 mm below the aortic annulus and directed toward the left ventricular apex. The first incision is made just to the right of the midpoint of the right coronary cusp and the second incision approximately 1 cm to the left, just below the commissure between the left and right coronary cusps. The intervening bar of muscle is then excised with countertraction applied to the previously placed stay suture.

ASA was performed using previously described techniques [10,16]. Briefly, a temporary pacemaker lead is inserted in all patients without permanent pacing devices. Measurements of LVOT gradient are recorded at rest, after extrasystole, and during Valsalva maneuver. An angioplasty balloon is introduced over a coronary wire into the septal perforator artery. After inflation of balloon, angiographic contrast is injected through the balloon catheter to identify the course of the septal artery and confirm lack of reflux proximal to balloon. Echocardiography is performed and gradients are measured during balloon inflation. Subsequently, a small volume of ethanol is injected slowly through the balloon catheter, followed by normal saline flush. Ten minutes after the last injection of ethanol, the balloon is deflated and removed. Coronary angiography excludes left anterior descending artery damage and verifies septal artery occlusion. Hemodynamic measurements are repeated. For patients with $\leq$50% reduction of LVOT gradient, targeting of other septal perforators is considered.

Implantable cardioverter defibrillators (ICD) were placed in accordance with standard guidelines at the time of the procedure, be that for primary or secondary prevention of sudden cardiac death. Patients with ICD's prior to septal reduction therapy were accounted for as well as those who had the devices inserted peri-procedurally or after 30 days [17–20].

Follow-up details of NYHA functional class and echocardiographic data, along with the need for repeat septal reduction therapy, were obtained by reviewing patient records, from information supplied by referring physicians, and mailed patient questionnaires. The most recent vital status was obtained for each of the study patients by interrogation of patient records and the Social Security Death Index.

Continuous values are presented as a mean $\pm$ standard deviation. These continuous values were compared with Student's *t*-test. The observed mortality rates of the myectomy and ASA cohorts were compared with expected mortality rates using the US Census Bureau 2002 national life-tables by means of a 1-sample log-rank test [21]. Comparisons with an age-matched population were carried out by means of standardized mortality ratio (SMR) [21].

Cumulative event rates were calculated according to the Kaplan–Meier method, with all-event or censoring times measured from the time of enrolment. The significance of differences in mortality between the groups was assessed with the use of the log-rank test.

Results

The baseline characteristics of our cohort are presented in Table 1. Analysis of the 5 years of data from the ASA cohort and 20 years in the surgical myectomy cohort was performed, and due to length of data, there are considerably fewer patients in the ASA group vs myectomy group (52 vs 171, respectively; Table 1). Subjects in the ASA group were generally older, with age ranges that overlapped the subjects in the surgical groups (57.3 $\pm$ 12.9 years vs 48.0 $\pm$ 17.1 years), and were more likely to be male (56% vs 49%). The ASA cohort was similar to the myectomy cohort with regards to initial NYHA class (2.99 $\pm$ 0.35 vs 2.74 $\pm$ 0.65), pre-procedural septal thickness (2.13 $\pm$ 0.45 mm vs 2.19 $\pm$ 0.60 mm), resting (67.1 $\pm$ 26.9 mmHg vs 67.4 $\pm$ 43.4 mmHg) and provoked LVOT gradients (104.4 $\pm$ 34.9 mmHg vs 98.1 $\pm$ 34.7 mmHg), mitral regurgitation (1.68 $\pm$ 0.7 vs 1.48 $\pm$ 1.0), and presence of systolic anterior motion of the mitral valve (95% vs 85%). Six patients in the ASA group had previously undergone ICD implantation, and this was done in accordance with the guidelines at the time of the procedure and follow-up [17–20]. None of the patients in the surgical cohort had ICDs placed prior to their procedure.

Table 1
Baseline characteristics of both treatment groups, pre-intervention (alcohol septal ablation or surgical myectomy) NYHA, New York Heart Association; LVOT, left ventricular outflow tract; ICD, implantable cardioverter defibrillator.

Baseline characteristics	Alcohol septal ablation	Surgical myectomy
Number of subjects	52	171
Age (years)	57.3 $\pm$ 12.9	48.0 $\pm$ 17.1
Sex (% men)	56	49
NYHA Class	2.99 $\pm$ 0.35	2.74 $\pm$ 0.65
Septal thickness (cm)	2.13 $\pm$ 0.45	2.19 $\pm$ 0.60
LVOT gradient-rest (mmHg)	67.1 $\pm$ 26.9	67.4 $\pm$ 43.4
LVOT gradient-provoked (mmHg)[a]	104.4 $\pm$ 34.9	98.1 $\pm$ 34.7
Mitral regurgitation	1.68 $\pm$ 0.7	1.48 $\pm$ 1.0
Systolic anterior motion (%)	95	85
ICD previously inserted (%)	11.5	0

[a] In the surgical myectomy group on 148 patients with a complete echocardiographic assessment.

Analysis of the procedures, both ASA and surgical myectomy, demonstrated similar characteristics to previously published data (Table 2). For the ASA cohort, the amount of alcohol injected was 3.28 $\pm$ 1.89 ml in a mean of 1.38 $\pm$ 0.60 septal arteries. The peak rises in creatinine kinase (CK) and creatinine kinase-MB (CK-MB) were 1656 $\pm$ 967 IU/L and 243 $\pm$ 138 IU/L, respectively. For the surgical myectomy cohort, the mean cross-clamp time was 23.2 $\pm$ 10.6 min, with mean cardiopulmonary bypass time 55.0 $\pm$ 16.3 min.

Peri-procedural outcomes were defined as those appearing up to 30 days after the procedure. Thirty-day events after the procedures were comparable to published data (Table 2) [4,12,13]. The mean rate of pacemaker placement was 7.7% for the ASA group and 6.4% for the surgical myectomy group. Likewise, the percentage of implantable cardioverter defibrillators placed peri-procedurally was 1.9% in the ASA cohort and 0% in the surgical myectomy group. Tamponade occurred in 1.9% of ASA patients. In the ASA group, there were no non-localized, large, remote myocardial infarctions or cerebrovascular events. Thirty-day mortality was 0.0% in the ASA cohort and 2.9% in the surgical myectomy cohort. No peri-procedural deaths after septal reduction procedures have occurred since 1994 at this institution.

Table 2
Individualized procedural characteristics, including overlapping statistics including rate of pacemaker placement, ICD placement, and short-term mortality for both procedures.

Procedural	Alcohol septal ablation	Surgical myectomy
Alcohol amount (ml)	3.28 $\pm$ 1.89	–
# Septals ablated	1.38 $\pm$ 0.60	–
CK	1656 $\pm$ 967	–
CK-MB	243 $\pm$ 138	–
CPB time (min)	–	55.0 $\pm$ 16.3
Crossclamp time (min)	–	23.2 $\pm$ 10.6
Peri-procedure PPM (%)	7.7	6.4
Peri-procedure ICD (%)	1.9	0
30-day mortality (%)	0	2.9

CK, creatinine kinase; CK-MB, MB fraction creatinine kinase; CPB, cardiopulmonary bypass; PPM, permanent pacemaker; ICD, implantable cardioverter defibrillator.

Table 3
Post-procedural characteristics including length of follow-up and changes in dimension and functional parameters.

Follow-up characteristics	Alcohol septal ablation	Surgical myectomy
Mean follow-up (years)	3.2	13.7
NYHA class	1.5 ± 0.74	1.54 ± 0.74
Septal thickness (cm)	1.55 ± 0.30	1.78 ± 0.66
LVOT gradient-rest (mm Hg)	23.9 ± 29.4	11.2 ± 16.4
LVOT gradient-provoked (mm Hg)	35.5 ± 38.6	33.6 ± 34.9
Mitral regurgitation	1.3 ± 0.7	1.24 ± 0.7
Systolic anterior motion (%)	69	61

NYHA, New York Heart Association; LVOT, left ventricular outflow tract.

For the follow-up of both groups (mean of 3.2 years for ASA, 13.7 years for surgical myectomy, Table 3), hemodynamics and symptoms post-procedurally were improved. Post-procedural echocardiography demonstrated improved resting LVOT gradients (67.1 ± 26.9 mmHg to 23.9 ± 29.4 mmHg for ASA, $p < 0.001$; 67.4 ± 43.4 mmHg to 11.2 ± 16.4 mm Hg for surgical myectomy, $p < 0.001$), and provoked LVOT gradients (104.4 ± 34.9 mmHg to 35.5 ± 38.6 mmHg for ASA, $p < 0.001$; 98.1 ± 34.7 mmHg to 33.6 ± 34.9 mm Hg for surgical myectomy, $p < 0.001$). In both cohorts, a significant difference between the pre- and post-procedural NYHA class was found (2.99 ± 0.35 to 1.5 ± 0.74 for ASA, $p < 0.001$, 2.74 ± 0.65 to 1.54 ± 0.74, $p < 0.001$). Values for mitral regurgitation (MR) (1.68 ± 0.7 to 1.3 ± 0.7 for ASA, $p = 0.003$; 1.48 ± 1.0 to 1.24 ± 0.7 for surgical myectomy, $p = 0.4$) and percentage of patients with systolic anterior motion (SAM) of the mitral valve (95%–69% for ASA, $p = 0.003$; 85%–69% for surgical myectomy, $p = 0.02$) improved with both therapies. These data are consistent with previously published data [4,12,13,16].

At the end of follow-up, a total of 14 patients in the ASA cohort had undergone ICD implantation, along with four patients in the surgical group, according to guidelines [17–20].

After 5, 10, 15, and 20 years of follow-up, survival was 92.9%, 81.1%, 68.9%, and 47.5%, respectively. At a long-term follow-up, the overall mortality of the myectomy cohort was significantly greater than that of an age-matched US general population (SMR = 1.40, $p < 0.005$; Fig. 2).

At 2 and 5 years post-procedure, observed survival for the ASA cohort was 97.8% and 94.7%, respectively (Fig. 3). Life-table analysis vs age-matched controls revealed no difference between the ASA cohort and the general population (SMR = 0.61, $p = 0.48$; Fig. 3). Nevertheless, given the small number of patients and short-term follow-up, larger and longer-term study is needed to make more definitive conclusions for this procedure.

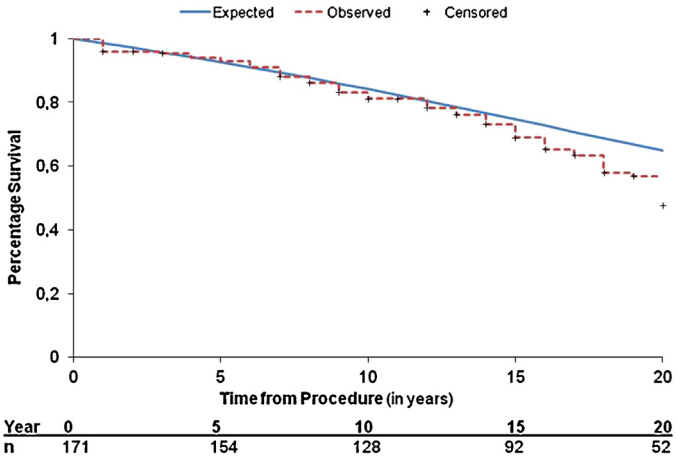

Fig. 2. Comparison of survival of surgical myectomy cohort (dashed line) vs age-matched controls from the US Census Bureau Data ($p < 0.005$).

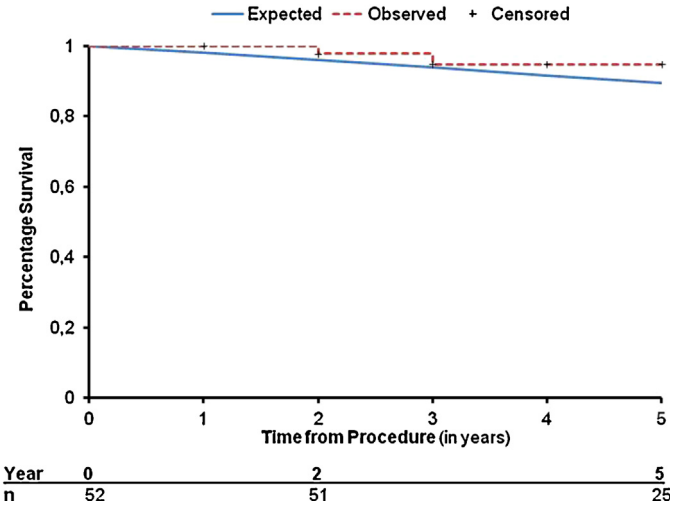

Fig. 3. Comparison of survival of alcohol septal ablation cohort (dashed line) vs age-matched controls from the US Census Bureau life table data ($p = 0.48$).

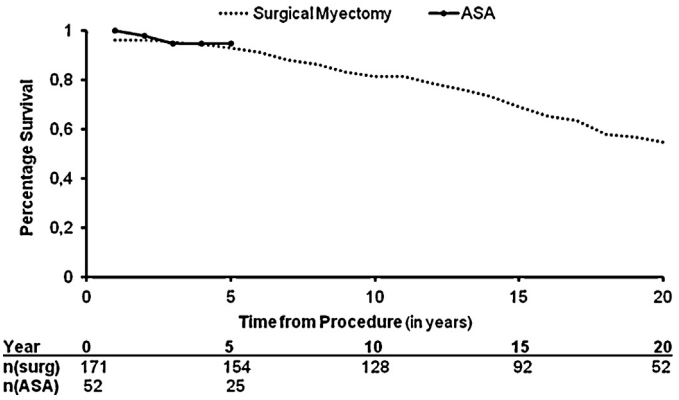

Fig. 4. Comparison of survival of alcohol septal ablation (ASA) vs surgical myectomy cohorts (hazard ratio 0.991, chi square = 0.0003, $p = 0.987$).

Fig. 4 represents the long-term survival of patients treated with ASA vs myectomy.

Discussion

In our paper, we present to our knowledge, the longest follow-up data on patients undergoing septal reduction therapy, 20 years (mean 13.7 years) for surgical myectomy and 5 years (mean of 3.2 years) for ASA. Historically, HCM patients were believed to exhibit annual death rates as high as 3–6%, with fatal arrhythmias and progressive heart failure contributing to poor outcome [22–24]. Although evidence has emerged that in unselected populations, the presence of HCM alone does not significantly adversely affect survival, the presence of obstruction, severe symptoms, atrial fibrillation, or marked left ventricular wall thickness identified populations at risk for increased mortality [1]. Maron and colleagues showed that presence of LVOT at rest, defined as basal gradient of at least 30 mmHg, is a strong, independent predictor of death [2]. Over the past four decades, septal myectomy has been the gold standard for amelioration of LVOT gradient and relief of symptoms in HCM patients [25–29]. Whether this improvement of ventricular hemodynamics translates into survival benefit has been difficult to determine based on lack of randomized controlled trials. However, in a seminal retrospective study of 289 patients

who underwent isolated surgical myectomy at the Mayo Clinic between 1983 and 2001, Ommen and colleagues [5] reported survival after myectomy at 5 and 10 years of 96% and 83%, respectively, compared with 79% and 61%, respectively, in non-operated patients with LVOT obstruction. Additionally, in that series with mean follow-up 5.8 years, survival after surgical myectomy did not differ significantly from age- and sex-matched general US population implying that surgical myectomy may favorably affect the survival of HCM patients.

Since its introduction in 1994, ASA has emerged as an alternative treatment strategy for obstruction in some HCM patients with symptoms unrelieved by optimal medical therapy. Although ASA may be associated with less complete resolution of LVOT gradient and with higher rates of pacemaker requirement than surgical myectomy (as high as 20% in some studies [6]) evidence has emerged that ASA is an effective procedure to lower outflow gradient and improve symptoms [30–34].

In the present study, we describe the outcomes of surgical myectomy and percutaneous ASA performed over 20 years and 5 years at Stanford Hospital for patients with symptomatic LVOT. We present data from 171 patients who underwent isolated septal myectomy and 52 patients who underwent ASA between January 1972 and December 2006. Although the decision to undergo myectomy or ASA was not randomized, the study represents real-world integration of the clinical judgment of an interdisciplinary team and patient preference at a tertiary referral center involved in the critical assessment of treatment modalities for HCM.

The principal findings of this nonrandomized, retrospective report are the following. First, both myectomy and ASA markedly improved NYHA functional classification and effectively reduced LVOT gradient. Secondly, 30-day mortality was low for both cohorts (0% for ASA, 2.9% for myectomy) despite inclusion of data from the early learning phase for each procedure at our institution. With respect to procedural complications, the overall low rate (7.7%) for pacemaker placement in the ASA cohort compares favorably with data from previously published reports [5,6,31,32] and may reflect incorporation of procedural modifications (i.e. slower injection rate of alcohol) shown by Fernandes and associates [35] to be associated with lower incidence of pacemaker placement. Indeed, no peri-operative death has occurred since 1994 at this institution.

Thirdly, this investigation found no overall impairment in survival after both myectomy and ASA on short-term follow-up when compared to an age- and sex-matched general US population. Short-term (5-year) survival was 92.9% after myectomy and 94.7% after ASA. These numbers compare favorably with the 5-year survival of 79% reported by Ommen and colleagues [5] for non-operated obstructive HCM patients. Although we cannot directly assess the effect of these treatments on mortality, our data suggest a potential early survival benefit in septal reduction procedures, both surgical and percutaneous, for properly selected patients with symptomatic obstructive HCM. Moreover, concern that the intramyocardial scar produced by ASA may contribute to ventricular arrhythmias did not manifest in an early survival disadvantage. Indeed, short-term survival was similar between patients treated with myectomy and ASA. However, longer follow-up will be necessary to clarify the risk of sudden death in this cohort.

Lastly, long-term mortality after myectomy was higher than for an age-matched general US population, but still compared favorably with historical data from non-operated HCM patients. We report survival after myectomy at 5, 10, 15, and 20 years at 92.9%, 81.1%, 68.9%, and 47.5%, respectively. Historical data on outcomes of non-operated HCM patients include 10-year survival of 61% as reported by Ommen and colleagues [5] for the subset of patients with basal LVOT gradient $\geq$30 mmHg. The lower mortality in our myectomy cohort suggests that surgical relief of LVOT obstruction in symptomatic patients may improve long-term survival. Conversely, the failure of myectomy to completely abolish a late survival disadvantage for HCM patients compared to the general population may reflect such factors as incomplete LVOT reduction, inability to abrogate diastolic dysfunction, or continued arrhythmogenic potential. Alternatively, the presence of obstruction may define a group with poorer long-term outcome even in spite of therapy.

Limitations of the present study include its nonrandomized, retrospective nature. Since cause of death was not available to us in the majority of myectomy cases, we were not able to assess survival free from HCM-related death. As a referral institution, follow-up for all of our patients was not always as complete as desired, and it is possible a small number patients may have had unreported of septal reduction therapies which were unaccounted for. As follow-up was also often directed by referring physician, a complete record of ICD implantation is also unavailable. Nevertheless, comparison of survival free from all-cause mortality of our myectomy and ASA cohorts with the US general population yielded data we regard as valid and clinically relevant.

Conclusion

Results of the present study indicate that both myectomy and ASA are safe and effective for relief of symptoms and reduction of LVOT gradient in symptomatic HCM. Short-term survival after myectomy and ASA is comparable to that of the US general population, while long-term survival after myectomy appears intermediate between the general population and non-operated obstructive HCM patients. These survival trends suggest that interventional treatment of LVOT gradient, both surgical and percutaneous, may improve survival in patients with symptomatic LVOT obstruction. However, longer follow-up is needed for a definitive evaluation of the outcomes after ASA, and further investigation into the long-term prognosis following more extensive current myectomy techniques is warranted.

Disclosures

There are no disclosures for the present paper.

References

[1] Maron BJ, Casey SA, Poliac LC, Gohman TE, Almquist AK, Aeppli DM. Clinical course of hypertrophic cardiomyopathy in a regional United States cohort. JAMA 1999;281:650–5.
[2] Maron MS, Olivotto I, Betocchi S, Casey SA, Lesser JR, Losi MA, Cecchi F, Maron BJ. Effect of left ventricular outflow tract obstruction on clinical outcome in hypertrophic cardiomyopathy. N Engl J Med 2003;348:295–303.
[3] Morrow AG, Brockenbrough EC. Surgical treatment of idiopathic hypertrophic subaortic stenosis: technic and hemodynamic results of subaortic ventriculomyotomy. Ann Surg 1961;154:181–9.
[4] Robbins RC, Stinson EB. Long-term results of left ventricular myotomy and myectomy for obstructive hypertrophic cardiomyopathy. J Thorac Cardiovasc Surg 1996;111:586–94.
[5] Ommen SR, Maron BJ, Olivotto I, Maron MS, Cecchi F, Betocchi S, Gersh BJ, Ackerman MJ, McCully RB, Dearani JA, Schaff HV, Danielson GK, Tajik AJ, Nishimura RA. Long-term effects of surgical septal myectomy on survival in patients with obstructive hypertrophic cardiomyopathy. J Am Coll Cardiol 2005;46:470–6.
[6] Ralph-Edwards A, Woo A, McCrindle BW, Shapero JL, Schwartz L, Rakowski H, Wigle ED, Williams WG. Hypertrophic obstructive cardiomyopathy: comparison of outcomes after myectomy or alcohol ablation adjusted by propensity score. J Thorac Cardiovasc Surg 2005;129:351–8.
[7] Sigwart U. Non-surgical myocardial reduction for hypertrophic obstructive cardiomyopathy. Lancet 1995;346:211–4.
[8] Alam M, Dokainish H, Lakkis N. Alcohol septal ablation for hypertrophic obstructive cardiomyopathy: a systematic review of published studies. J Interv Cardiol 2006;19:319–27.

[9] Qin JX, Shiota T, Lever HM, Kapadia SR, Sitges M, Rubin DN, Bauer F, Greenberg NL, Agler DA, Drinko JK, Martin M, Tuzcu EM, Smedira NG, Lytle B, Thomas JD. Outcome of patients with hypertrophic obstructive cardiomyopathy after percutaneous transluminal septal myocardial ablation and septal myectomy surgery. J Am Coll Cardiol 2001;38:1994–2000.
[10] Firoozi S, Elliott PM, Sharma S, Murday A, Brecker SJ, Hamid MS, Sachdev B, Thaman R, McKenna WJ. Septal myotomy-myectomy and transcoronary septal alcohol ablation in hypertrophic obstructive cardiomyopathy. A comparison of clinical, haemodynamic and exercise outcomes. Eur Heart J 2002;23:1617–24.
[11] Nagueh SF, Ommen SR, Lakkis NM, Killip D, Zoghbi WA, Schaff HV, Danielson GK, Quinones MA, Tajik AJ, Spencer WH. Comparison of ethanol septal reduction therapy with surgical myectomy for the treatment of hypertrophic obstructive cardiomyopathy. J Am Coll Cardiol 2001;38:1701–6.
[12] van der Lee C, ten Cate FJ, Geleijnse ML, Kofflard MJ, Pedone C, van Herwerden LA, Biagini E, Vletter WB, Serruys PW. Percutaneous versus surgical treatment for patients with hypertrophic obstructive cardiomyopathy and enlarged anterior mitral valve leaflets. Circulation 2005;112:482–8.
[13] Mohr R, Schaff HV, Danielson GK, Puga FJ, Pluth JR, Tajik AJ. The outcome of surgical treatment of hypertrophic obstructive cardiomyopathy. Experience over 15 years. J Thorac Cardiovasc Surg 1989;97:666–74.
[14] Nagueh SF, Bierig SM, Budoff MJ, Desai M, Dilsizian V, Eidem B, Goldstein SA, Hung J, Maron MS, Ommen SR, Woo A. American Society of Echocardiography clinical recommendations for multimodality cardiovascular imaging of patients with hypertrophic cardiomyopathy: endorsed by the American Society of Nuclear Cardiology. Society for Cardiovascular Magnetic Resonance, and Society of Cardiovascular Computed Tomography. J Am Soc Echocardiogr 2011;24:473–98.
[15] Rickham PP. Human experimentation. Code of ethics of the world medical association. Declaration of Helsinki. Br Med J 1964;2:177.
[16] Holmes Jr DR, Valeti US, Nishimura RA. Alcohol septal ablation for hypertrophic cardiomyopathy: indications and technique. Catheter Cardiovasc Interv 2005;66:375–89.
[17] Epstein AE, DiMarco JP, Ellenbogen KA, Estes III NA, Freedman RA, Gettes LS, Gillinov AM, Gregoratos G, Hammill SC, Hayes DL, Hlatky MA, Newby LK, Page RL, Schoenfeld MH, Silka MJ, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices): developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. Circulation 2008;117:e350–408.
[18] Gregoratos G, Cheitlin MD, Conill A, Epstein AE, Fellows C, Ferguson Jr TB, Freedman RA, Hlatky MA, Naccarelli GV, Saksena S, Schlant RC, Silka MJ. ACC/AHA guidelines for implantation of cardiac pacemakers and antiarrhythmia devices: executive summary—a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (committee on pacemaker implantation). Circulation 1998;97:1325–35.
[19] Pelliccia A, Zipes DP, Maron BJ. Bethesda Conference #36 and the European Society of Cardiology consensus recommendations revisited a comparison of U.S. and European criteria for eligibility and disqualification of competitive athletes with cardiovascular abnormalities. J Am Coll Cardiol 2008;52:1990–6.
[20] Maron BJ, McKenna WJ, Danielson GK, Kappenberger LJ, Kuhn HJ, Seidman CE, Shah PM, Spencer 3rd WH, Spirito P, Ten Cate FJ, Wigle ED. American College of Cardiology/European Society of Cardiology clinical expert consensus document on hypertrophic cardiomyopathy. A report of the American College of Cardiology Foundation Task Force on clinical expert consensus documents and the European Society of Cardiology committee for practice guidelines. J Am Coll Cardiol 2003;42:1687–713.
[21] Finkelstein DM, Muzikansky A, Schoenfeld DA. Comparing survival of a sample to that of a standard population. J Natl Cancer Inst 2003;95:1434–9.
[22] Hardarson T, De la Calzada CS, Curiel R, Goodwin JF. Prognosis and mortality of hypertrophic obstructive cardiomyopathy. Lancet 1973;2:1462–7.
[23] Shah PM, Adelman AG, Wigle ED, Gobel FL, Burchell HB, Hardarson T, Curiel R, De La Calzada C, Oakley CM, Goodwin JF. The natural (and unnatural) history of hypertrophic obstructive cardiomyopathy. Circ Res 1974;35(Suppl. II): 179–95.
[24] Braunwald E, Lambrew CT, Rockoff SD, Ross Jr J, Morrow AG. Idiopathic hypertrophic subaortic stenosis. I. A description of the disease based upon an analysis of 64 patients. Circulation 1964;30(Suppl. 4):3–119.
[25] Williams WG, Wigle ED, Rakowski H, Smallhorn J, LeBlanc J, Trusler GA. Results of surgery for hypertrophic obstructive cardiomyopathy. Circulation 1987;76: V104–8.
[26] Morrow AG, Reitz BA, Epstein SE, Henry WL, Conkle DM, Itscoitz SB, Redwood DR. Operative treatment in hypertrophic subaortic stenosis. Techniques, and the results of pre and postoperative assessments in 83 patients. Circulation 1975;52:88–102.
[27] Schulte HD, Borisov K, Gams E, Gramsch-Zabel H, Losse B, Schwartzkopff B. Management of symptomatic hypertrophic obstructive cardiomyopathy—long-term results after surgical therapy. Thorac Cardiovasc Surg 1999;47: 213–8.
[28] McCully RB, Nishimura RA, Tajik AJ, Schaff HV, Danielson GK. Extent of clinical improvement after surgical treatment of hypertrophic obstructive cardiomyopathy. Circulation 1996;94:467–71.
[29] Dearani JA, Ommen SR, Gersh BJ, Schaff HV, Danielson GK. Surgery insight: septal myectomy for obstructive hypertrophic cardiomyopathy—the Mayo Clinic experience. Nat Clin Pract Cardiovasc Med 2007;4:503–12.
[30] Alam M, Dokainish H, Lakkis NM. Hypertrophic obstructive cardiomyopathy-alcohol septal ablation vs. myectomy: a meta-analysis. Eur Heart J 2009; 30:1080–7.
[31] Knight CJ. Alcohol septal ablation for obstructive hypertrophic cardiomyopathy. Heart 2006;92:1339–44.
[32] Schonbeck MH, Brunner-La Rocca HP, Vogt PR, Lachat ML, Jenni R, Hess OM, Turina MI. Long-term follow-up in hypertrophic obstructive cardiomyopathy after septal myectomy. Ann Thorac Surg 1998;65:1207–14.
[33] Sorajja P, Valeti U, Nishimura RA, Ommen SR, Rihal CS, Gersh BJ, Hodge DO, Schaff HV, Holmes Jr DR. Outcome of alcohol septal ablation for obstructive hypertrophic cardiomyopathy. Circulation 2008;118:131–9.
[34] Seggewiss H, Gleichmann U, Faber L, Fassbender D, Schmidt HK, Strick S. Percutaneous transluminal septal myocardial ablation in hypertrophic obstructive cardiomyopathy: acute results and 3-month follow-up in 25 patients. J Am Coll Cardiol 1998;31:252–8.
[35] Fernandes VL, Nielsen C, Nagueh SF, Herrin AE, Slifka C, Franklin J, Spencer 3rd WH. Follow-up of alcohol septal ablation for symptomatic hypertrophic obstructive cardiomyopathy the Baylor and Medical University of South Carolina experience 1996 to 2007. JACC Cardiovasc Interv 2008;1: 561–70.